Remarks

By way of this Preliminary Amendment, claims 1-13, 16-23 and 28 are pending. Claims 14, 15 and 24-27 have been canceled, and claims 1-13, 16, 17, 19, 20 and 22 have been amended. New claim 28 has been added. These claim cancellations, amendments and additions are being made solely for purposes of placing the claims in a format appropriate for U.S. prosecution. No new matter was added by way of these claim amendments and additions.

More specifically, claims 1-13 are being amended to convert the Swiss-type use claim to the U.S. method of treatment format. Claim 16 is being amended to remove the improper multiple dependent claim format in compliance with 37 C.F.R. § 1.75(c) and to make it independent by adding material from claim 1. Claim 17 is being amended to separate the claim into two claims. Material deleted from claim 17 has been rewritten in dependent form in new claim 28. Finally, claims 19, 20 and 22 are being amended to specify that "Y" is as defined in claim 16 and to change claim dependencies. Applicants submit that all of these amendments do not change the scope of the claims as originally filed, because the amendments are being made solely to place the claims in a format appropriate for U.S. prosecution. Such amendments are therefore made to address formalities in the claim format and are not related to the patentability of the subject matter of the claims.

Conclusion

Applicants believe that the subject matter of the pending claims is patentable and that the instant application should accordingly be allowed. If the Examiner believes that a conversation with Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned attorney at (203) 812-3964.

Respectfully submitted,

Dated: July 24, 2001

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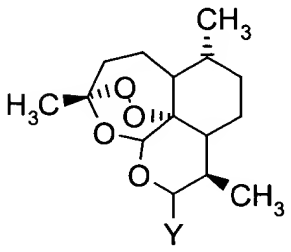
Amended Claims for U.S.S.N. 09/743,827 (Attorney Docket No. Le A 33 820)

a1

1. (Amended) A method of treating or preventing a disease caused by infection with a parasite other than an organism of the genus Plasmodium, comprising administering to a host in need thereof an effective amount of a compound of the general formula I



(I)

or a salt thereof,

in which

Y represents a halogen atom, an optionally substituted cycloalkyl, aryl, C-linked heteroaryl or heterocyclylalkyl group or a group $-NR^1R^2$; where

R^1 represents a hydrogen atom or an optionally substituted alkyl, alkenyl or alkynyl group;

R^2 represents an optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl or aralkyl group; or

R^1 and R^2 together with the interjacent nitrogen atom represent an optionally substituted heterocyclic group or an amino group derived from an optionally substituted amino acid ester.

2. (Amended) The method of claim 1, in which Y represents a halogen atom.

3. (Amended) The method of claim 2, in which Y represents a fluorine or bromine atom.

A'cont

4. (Amended) The method of claim 1, in which Y represents a C_{3-8} cycloalkyl group, a C_{6-18} aryl group, a 5- to 10-membered C-linked heteroaryl group or a 5- to 10-membered heterocyclyl-C_{1-6} alkyl group, each group being optionally substituted by one or more substituents selected from the group consisting of halogen atoms, hydroxyl, C_{1-4} alkyl, C_{2-4} alkenyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, carboxyl, C_{6-10} aryl, 5 to 10-membered heterocyclic and C_{1-4} alkyl- or phenyl-substituted 5- to 10-membered heterocyclic groups.

5. (Amended) The method of claim 4, in which Y represents a C_{6-18} aryl group optionally substituted by one or more substituents selected from the group consisting of halogen atoms, hydroxyl, C_{1-4} alkyl, C_{2-4} alkenyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino and carboxyl groups.

6. (Amended) The method of claim 4, in which Y represents a phenyl, naphthyl, anthryl or phenanthryl group, each group being optionally substituted by one or more substituents selected from the group consisting of halogen atoms and hydroxyl, methyl, vinyl, C_{1-4} alkoxy and carboxyl groups.

7. (Amended) The method of claim 4, in which Y represents a phenyl, fluorophenyl chlorophenyl, bromophenyl, trimethylphenyl, vinylphenyl, methoxyphenyl, dimethoxyphenyl, trimethoxyphenyl, carboxylphenyl, naphthyl, hydroxynaphthyl, methoxynaphthyl, anthryl or phenanthryl group.

8. (Amended) The method of claim 7, in which Y represents a phenyl or trimethoxyphenyl group.

9. (Amended) The method of claim 1, in which Y represents a group $-NR^1R^2$ where R^1 represents a hydrogen atom or a C_{1-6} alkyl group and R^2 represents a C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl or C_{7-16} aralkyl group, or R^1 and R^2 together with the interjacent nitrogen atom represent a 5- to 10-membered heterocyclic group or an amino group derived from a C_{1-6} alkyl ester of an amino acid, each group being optionally substituted by one or more

Alcont.

substituents selected from the group consisting of halogen atoms, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-6} alkoxycarbonyl, phenyl, halophenyl, C_{1-4} alkylphenyl, C_{1-4} haloalkylphenyl, C_{1-4} alkoxyphenyl, benzyl, pyridyl and pyrimidinyl groups.

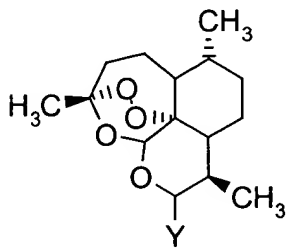
10. (Amended) The method of claim 9, in which Y represents a group $-NR^1R^2$ where R^1 represents a hydrogen atom or a C_{1-4} alkyl group and R^2 represents a C_{1-4} alkyl, C_{3-6} cycloalkyl, phenyl or benzyl group, or R^1 and R^2 together with the interjacent nitrogen atom represent a 6- to 10-membered heterocyclic group or an amino group derived from a C_{1-4} alkyl ester of an amino acid, each group being optionally substituted by one or more substituents selected from the group consisting of halogen atoms, C_{1-4} haloalkyl, C_{1-4} alkoxycarbonyl, phenyl, halophenyl, C_{1-4} alkylphenyl, C_{1-4} haloalkylphenyl, C_{1-4} alkoxyphenyl, benzyl, pyridyl and pyrimidinyl groups.

11. (Amended) The method of claim 9, in which Y represents a propylamino, cyclopentylamino, cyclohexylamino, phenylamino, fluorophenylamino, chlorophenylamino, bromophenylamino, iodophenylamino, methoxycarbonylphenylamino, biphenylamino, benzylamino, fluorobenzylamino, bis(trifluoromethyl)benzylamino, phenylethylamino, phenyl-methoxycarbonylmethylamino, diethylamino, morpholinyl, thiomorpholinyl, morpholinosulphonyl, indolinyl, tetrahydroisoquinolinyl, phenylpiperazinyl, fluorophenylpiperazinyl, chlorophenylpiperazinyl, methylphenylpiperazinyl, trifluoromethylphenylpiperazinyl, methoxyphenylpiperazinyl, benzylpiperazinyl, pyridylpiperazinyl and pyrimidinylpiperazinyl group.

12. (Amended) The method of claim 9, in which Y represents a propylamino, phenylamino, bromophenylamino, iodophenylamino, biphenylamino, benzylamino, bis(trifluoromethyl)benzylamino, phenylethylamino, phenyl-methoxycarbonylmethylamino or morpholinyl group.

13. (Amended) The method of claim 1, in which said parasite is an organism of the genus Neospora or the genus Eimeria.

16. (Amended) A compound of the general formula I



(I)

or a salt thereof,

in which

Y represents a halogen atom, an optionally substituted cycloalkyl, aryl, C-linked heteroaryl or heterocyclylalkyl group or a group $-NR^1R^2$; where

R^1 represents a hydrogen atom or an optionally substituted alkyl, alkenyl or alkynyl group;

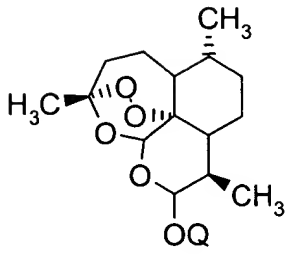
R^2 represents an optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl or aralkyl group; or

R^1 and R^2 together with the interjacent nitrogen atom represent an optionally substituted heterocyclic group or an amino group derived from an optionally substituted amino acid ester,

with the proviso that, when Y is a group $-NR^1R^2$ and R^2 represents a phenyl, 3-chlorophenyl, 4-chlorophenyl, 3-bromophenyl, 4-bromophenyl, 4-iodophenyl, 4-methylphenyl, 4-methoxyphenyl, 3-carboxylphenyl or 4-carboxylphenyl group, then R^1 is an optionally substituted alkyl group.

17. (Amended) A process for the preparation of a compound of the general formula I according to claim 16 which comprises reacting a compound of the general formula II

A2 cont



(II)

in which Q represents a hydrogen atom or trimethylsilyl group, with a suitable halogenating agent to form a compound of the general formula I in which Y represents a halogen atom.

A3

19. (Amended) A process for the preparation of a compound of the general formula I according to claim 16, in which Y represents an optionally substituted cycloalkyl, aryl, C-linked heteroaryl or heterocyclylalkyl group which comprises reacting 9,10-anhydroartemisinin with a compound of the general formula Y-H, where Y is as defined above in claim 16, in the presence of a Lewis acid.

20. (Amended) A process for the preparation of a compound of the general formula I according to claim 16, in which Y represents an optionally substituted aryl or C-linked heteroaryl group which comprises reacting 10-trichloroacetimidoyl-10-deoxoartemisinin with a compound of the general formula Y-H, where Y is as defined above in claim 16, in the presence of a Lewis acid.

A4

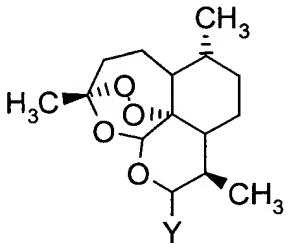
22. (Amended) A process for the preparation of a compound of the general formula I according to claim 16, in which Y represents an optionally substituted aryl or C-linked heteroaryl group which comprises reacting a 10-acyloxyartemisinin compound in which the acyloxy group is of formula A-(C=O)-O-, where A represents an optionally substituted alkyl, cycloalkyl, aryl, aralkyl, heterocyclic or polycyclic group, with a compound of the general formula Y-H, where Y is as defined above in claim 16, in the presence of a Lewis acid.

New Claim for U.S.S.N. 09/743,827 (Attorney Docket No. Le A 33 820)

28. (New) The process of claim 17, further comprising reacting the compound of general formula I thus formed either with a Grignard reagent of the general formula YMgX where Y is an optionally substituted cycloalkyl, aryl, C-linked heteroaryl or heterocyclylalkyl group and X is a halogen atom to form a compound of general formula I in which Y represents an optionally substituted cycloalkyl, aryl, C-linked heteroaryl or heterocyclylalkyl group or with an amine of the general formula HNR^1R^2 where R^1 and R^2 are as defined in claim 16 to form a compound of general formula I in which Y represents a group $-NR^1R^2$ where R^1 and R^2 are as defined above in claim 16.

Amended Claims for U.S.S.N. 09/743,827 (Attorney Docket No. Le A 33 820)
Version with Markings to Show Changes Made

1. (Amended) A method of treating or preventing a disease caused by infection with a parasite other than an organism of the genus Plasmodium, comprising administering to a host in need thereof an effective amount of a compound of the general formula I



(I)

or a salt thereof,

in which

Y represents a halogen atom, an optionally substituted cycloalkyl, aryl, C-linked heteroaryl or heterocyclylalkyl group or a group $-NR^1R^2$; where

R^1 represents a hydrogen atom or an optionally substituted alkyl, alkenyl or alkynyl group;

R^2 represents an optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl or aralkyl group; or

R^1 and R^2 together with the interjacent nitrogen atom represent an optionally substituted heterocyclic group or an amino group derived from an optionally substituted amino acid ester[;

for use in the treatment and/or prophylaxis of a disease caused by infection with a parasite other than an organism of the genus Plasmodium].

2. (Amended) The method of [A compound according to] claim 1 in which Y represents a halogen atom.

3. (Amended) The method of [A compound according to claim 1 or] claim 2 in which Y represents a fluorine or bromine atom.

4. (Amended) The method of [A compound according to] claim 1 in which Y represents a C_{3-8} cycloalkyl group, a C_{6-18} aryl group, a 5- to 10-membered C-linked heteroaryl group or a 5- to 10-membered heterocyclyl-C_{1-6} alkyl group, each group being optionally substituted by one or more substituents selected from the group consisting of halogen atoms, hydroxyl, C_{1-4} alkyl, C_{2-4} alkenyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, carboxyl, C_{6-10} aryl, 5 to 10-membered heterocyclic and C_{1-4} alkyl- or phenyl-substituted 5- to 10-membered heterocyclic groups.

5. (Amended) The method of [A compound according to] claim 4 in which Y represents a C_{6-18} aryl group optionally substituted by one or more substituents selected from the group consisting of halogen atoms, hydroxyl, C_{1-4} alkyl, C_{2-4} alkenyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino and carboxyl groups.

6. (Amended) The method of [A compound according to] claim 4 [or claim 5] in which Y represents a phenyl, naphthyl, anthryl or phenanthryl group, each group being optionally substituted by one or more substituents selected from the group consisting of halogen atoms and hydroxyl, methyl, vinyl, C_{1-4} alkoxy and carboxyl groups.

7. (Amended) The method of [A compound according to any one of] claim[s] 4 [to 6] in which Y represents a phenyl, fluorophenyl chlorophenyl, bromophenyl, trimethylphenyl, vinylphenyl, methoxyphenyl, dimethoxyphenyl, trimethoxyphenyl, carboxylphenyl, naphthyl, hydroxynaphthyl, methoxynaphthyl, anthryl or phenanthryl group.

8. (Amended) The method of [A compound according to any one of] claim[s 4 to] 7 in which Y represents a phenyl or trimethoxyphenyl group.

9. (Amended) The method of [A compound according to] claim 1 in which Y represents a group $-NR^1R^2$ where R^1 represents a hydrogen atom or a C_{1-6} alkyl group and R^2 represents a C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl or C_{7-16} aralkyl group, or R^1 and R^2 together with the interjacent nitrogen atom represent a 5- to 10-membered heterocyclic group or an amino group derived from a C_{1-6} alkyl ester of an amino acid, each group being optionally substituted by one or more substituents selected from the group consisting of halogen atoms, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-6} alkoxycarbonyl, phenyl, halophenyl, C_{1-4} alkylphenyl, C_{1-4} haloalkylphenyl, C_{1-4} alkoxyphenyl, benzyl, pyridyl and pyrimidinyl groups.

10. (Amended) The method of [A compound according to] claim 9 in which Y represents a group $-NR^1R^2$ where R^1 represents a hydrogen atom or a C_{1-4} alkyl group and R^2 represents a C_{1-4} alkyl, C_{3-6} cycloalkyl, phenyl or benzyl group, or R^1 and R^2 together with the interjacent nitrogen atom represent a 6- to 10-membered heterocyclic group or an amino group derived from a C_{1-4} alkyl ester of an amino acid, each group being optionally substituted by one or more substituents selected from the group consisting of halogen atoms, C_{1-4} haloalkyl, C_{1-4} alkoxycarbonyl, phenyl, halophenyl, C_{1-4} alkylphenyl, C_{1-4} haloalkylphenyl, C_{1-4} alkoxyphenyl, benzyl, pyridyl and pyrimidinyl groups.

11. (Amended) The method of [A compound according to] claim 9 [or claim 10] in which Y represents a propylamino, cyclopentylamino, cyclohexylamino, phenylamino, fluorophenylamino, chlorophenylamino, bromophenylamino, iodophenylamino, methoxycarbonylphenylamino, biphenylamino, benzylamino, fluorobenzylamino, bis(trifluoromethyl)benzylamino, phenylethylamino, phenyl-methoxycarbonylmethylamino, diethylamino, morpholinyl, thiomorpholinyl, morpholinosulphonyl, indolinyl, tetrahydroisoquinolinyl, phenylpiperazinyl, fluorophenylpiperazinyl, chlorophenylpiperazinyl, methylphenylpiperazinyl, trifluoromethylphenylpiperazinyl, methoxyphenylpiperazinyl, benzylpiperazinyl, pyridylpiperazinyl and pyrimidinylpiperazinyl group.

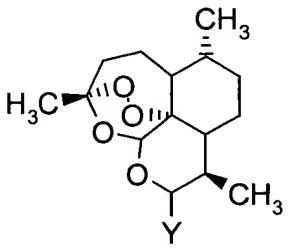
12. (Amended) The method of [A compound according to any one of] claim[s] 9 [to 11] in which Y represents a propylamino, phenylamino, bromophenylamino, iodophenylamino, biphenylamino, benzylamino, bis(trifluoromethyl)benzylamino, phenylethylamino, phenyl-methoxycarbonylmethylamino or morpholinyl group.

13. (Amended) The method of claim 1 [A compound according to any one of the preceding claims] in which the parasite is an organism of the genus Neospora or the genus Eimeria.

14. canceled.

15. canceled.

16. (Amended) A compound of the general formula I



(I)

or a salt thereof,

in which

Y represents a halogen atom, an optionally substituted cycloalkyl, aryl, C-linked heteroaryl or heterocyclylalkyl group or a group $-NR^1R^2$; where

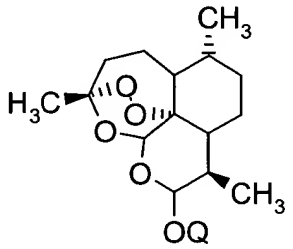
R^1 represents a hydrogen atom or an optionally substituted alkyl, alkenyl or alkynyl group;

R^2 represents an optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl or aralkyl group; or

R^1 and R^2 together with the interjacent nitrogen atom represent an optionally substituted heterocyclic group or an amino group derived from an optionally substituted amino acid ester

[as defined in any one of claims 1 to 12,] with the proviso that, when Y is a group -NR^1R^2 and R^2 represents a phenyl, 3-chlorophenyl, 4-chlorophenyl, 3-bromophenyl, 4-bromophenyl, 4-iodophenyl, 4-methylphenyl, 4-methoxyphenyl, 3-carboxylphenyl or 4-carboxylphenyl group, then R^1 is an optionally substituted alkyl group.

17. (Amended) A process for the preparation of a compound of the general formula I according to claim 16 which comprises reacting a compound of the general formula II



(II)

in which Q represents a hydrogen atom or trimethylsilyl group, with a suitable halogenating agent to form a compound of the general formula I in which Y represents a halogen atom[; and, if desired, reacting the compound of general formula I thus formed either with a Grignard reagent of the general formula YMgX where Y is an optionally substituted cycloalkyl, aryl, C-linked heteroaryl or heterocyclylalkyl group and X is a halogen atom to form a compound of general formula I in which Y represents an optionally substituted cycloalkyl, aryl, C-linked heteroaryl or heterocyclylalkyl group or with an amine of the general formula HNR^1R^2 where R^1 and R^2 are as defined in claim 13 to form a compound of general formula I in which Y represents a group -NR^1R^2 where R^1 and R^2 are as defined above].

19. (Amended) A process for the preparation of a compound of the general formula I according to claim 16 in which Y represents an optionally substituted cycloalkyl, aryl, C-linked heteroaryl or heterocyclylalkyl group which comprises

reacting 9,10-anhydroartemisinin with a compound of the general formula Y-H, where Y is as defined above in claim 16, in the presence of a [suitable] Lewis acid.

20. (Amended) A process for the preparation of a compound of the general formula I according to claim [1] 16 in which Y represents an optionally substituted aryl or C-linked heteroaryl group which comprises reacting 10-trichloroacetimidoyl-10-deoxoartemisinin with a compound of the general formula Y-H, where Y is as defined above in claim 16, in the presence of a [suitable] Lewis acid.

22. (Amended) A process for the preparation of a compound of the general formula I according to claim [1] 16 in which Y represents an optionally substituted aryl or C-linked heteroaryl group which comprises reacting a 10-acyloxyartemisinin compound in which the acyloxy group is of formula A- (C=O)-O-, where A represents an optionally substituted alkyl, cycloalkyl, aryl, aralkyl, heterocyclic or polycyclic group, with a compound of the general formula Y-H, where Y is as defined above in claim 16, in the presence of a Lewis acid.

24. canceled.

25. canceled.

26. canceled.

27. canceled.